The Health Effects of Polychlorinated Biphenyls
or
"How I learned to stop worrying and love the ban"

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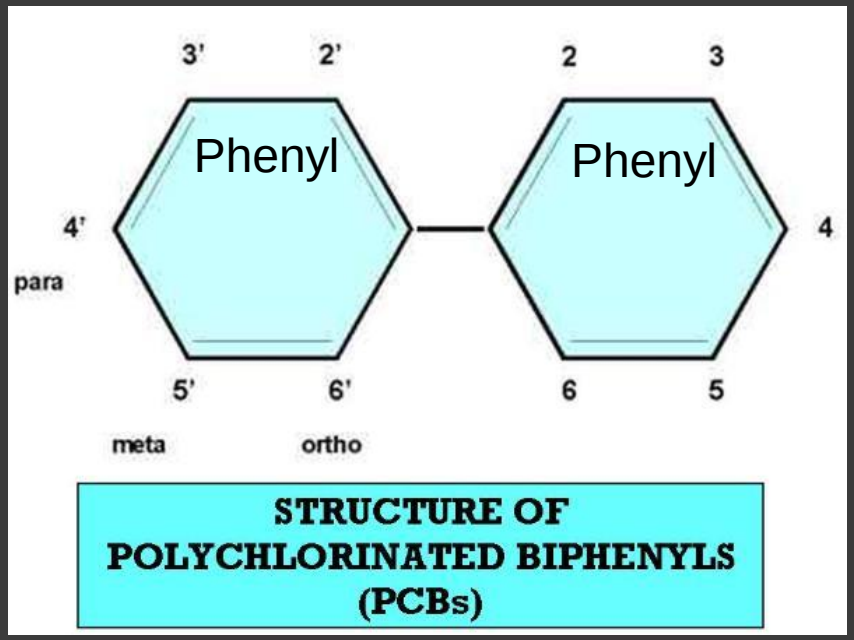
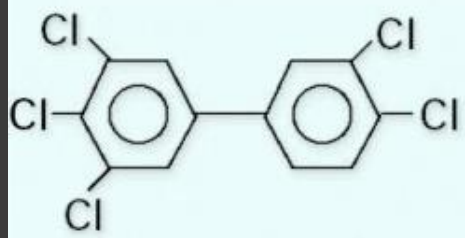
Outline

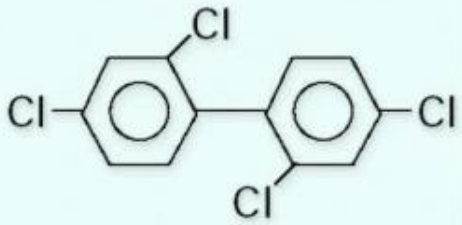
I. What are PCBs and why should we care?
II. Molecular mechanisms as a predictor of toxicity/carcinogenicity
    A. Activation of the Aryl Hydrocarbon Receptor (AhR)
    B. Activation of the Pregnone X (PXR) and Constitutive Androstone (CAR) receptors.
III. Some specific examples of PCB exposure health effects
    A. Endocrine/Reproductive disruption
    B. Neurotoxicity
    C. Immunotoxicity
    D. Carcinogenicity
IV. Helpful links

What Are PCBs?



PCBs are structurally distinct and have more than one mechanism of action





Coplanar PCBs	Noncoplanar PCBs
meta, para substituted	*ortho* substituted
Bind with high affinity to the Ah receptor	Are not good ligands for the Ah receptor
Mediate many effects through changes in gene transcription	Mechanisms of action are unknown but initiated by changes in cell signaling

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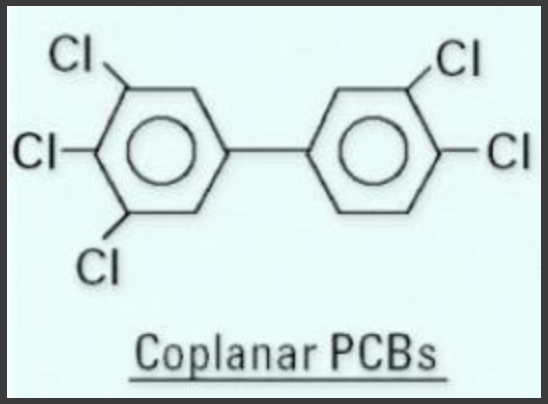
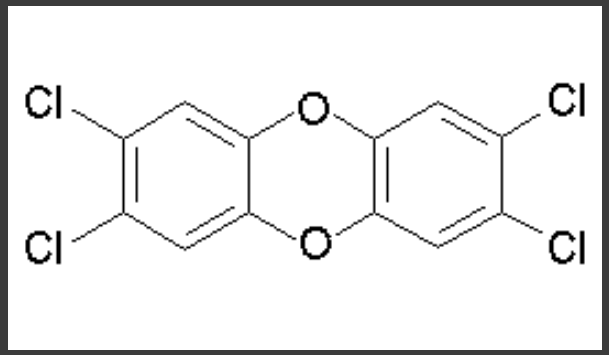
*www.isc-bio.org

Co-Planar (Flat) PCBs Look Like Dioxin





Dioxin

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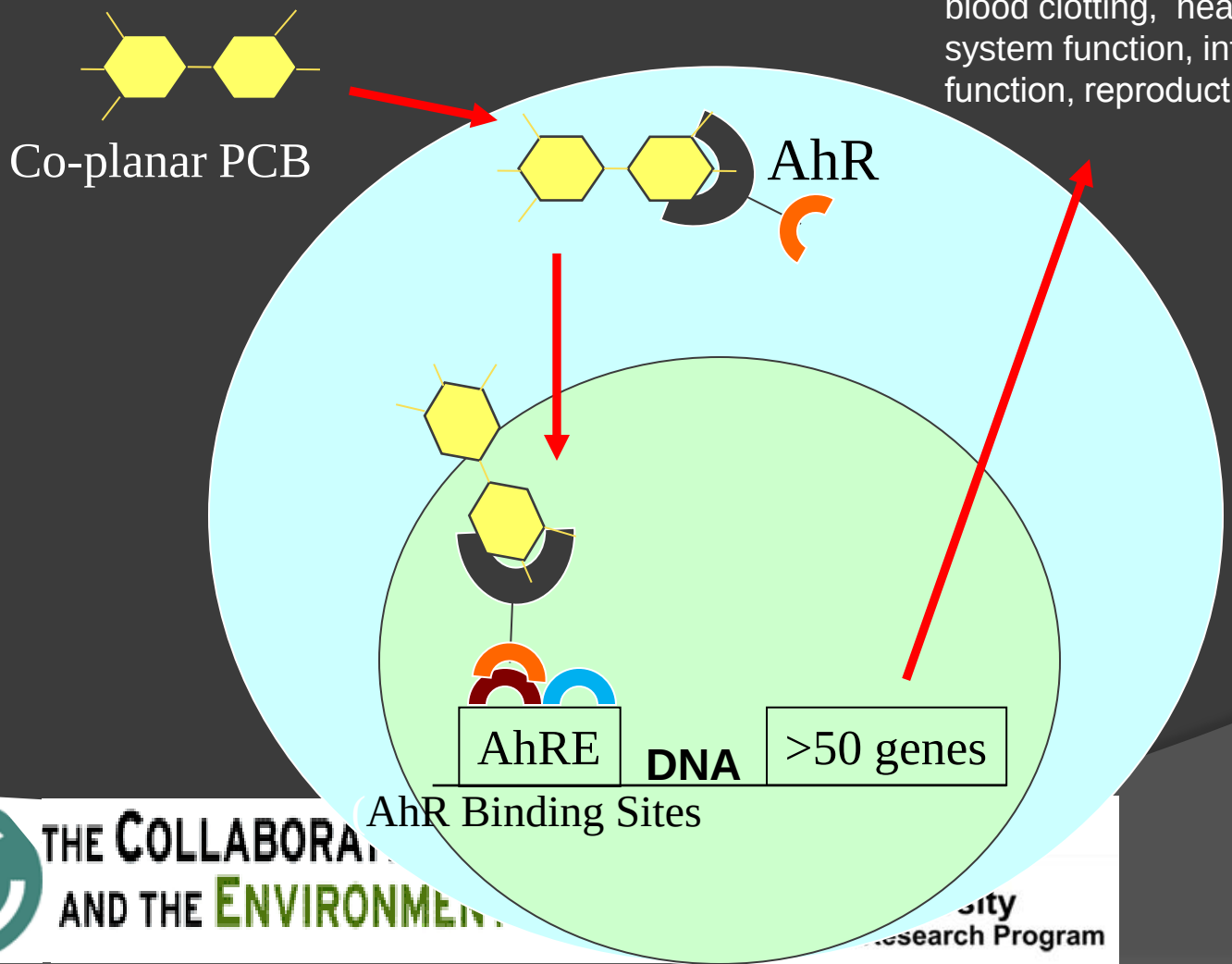
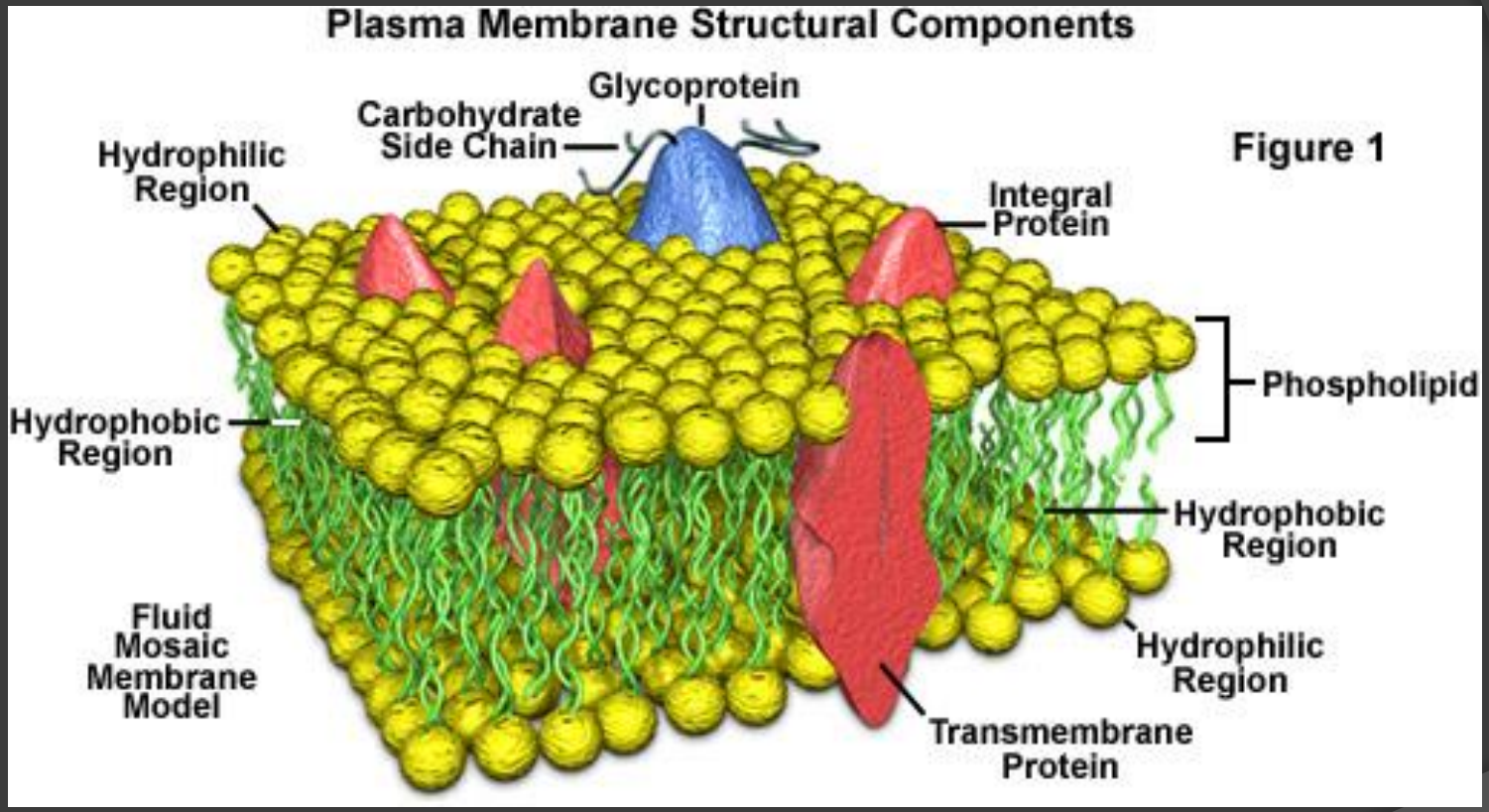
Planar PCBs and Dioxin Act Through a Protein Receptor (The AhR)

Growth, death, migration, hormone production, red blood cell development, blood clotting, heart development, immune system function, inflammation, neurologic function, reproduction…



Non-Planar PCBs Intercalate into the Cell Membrane



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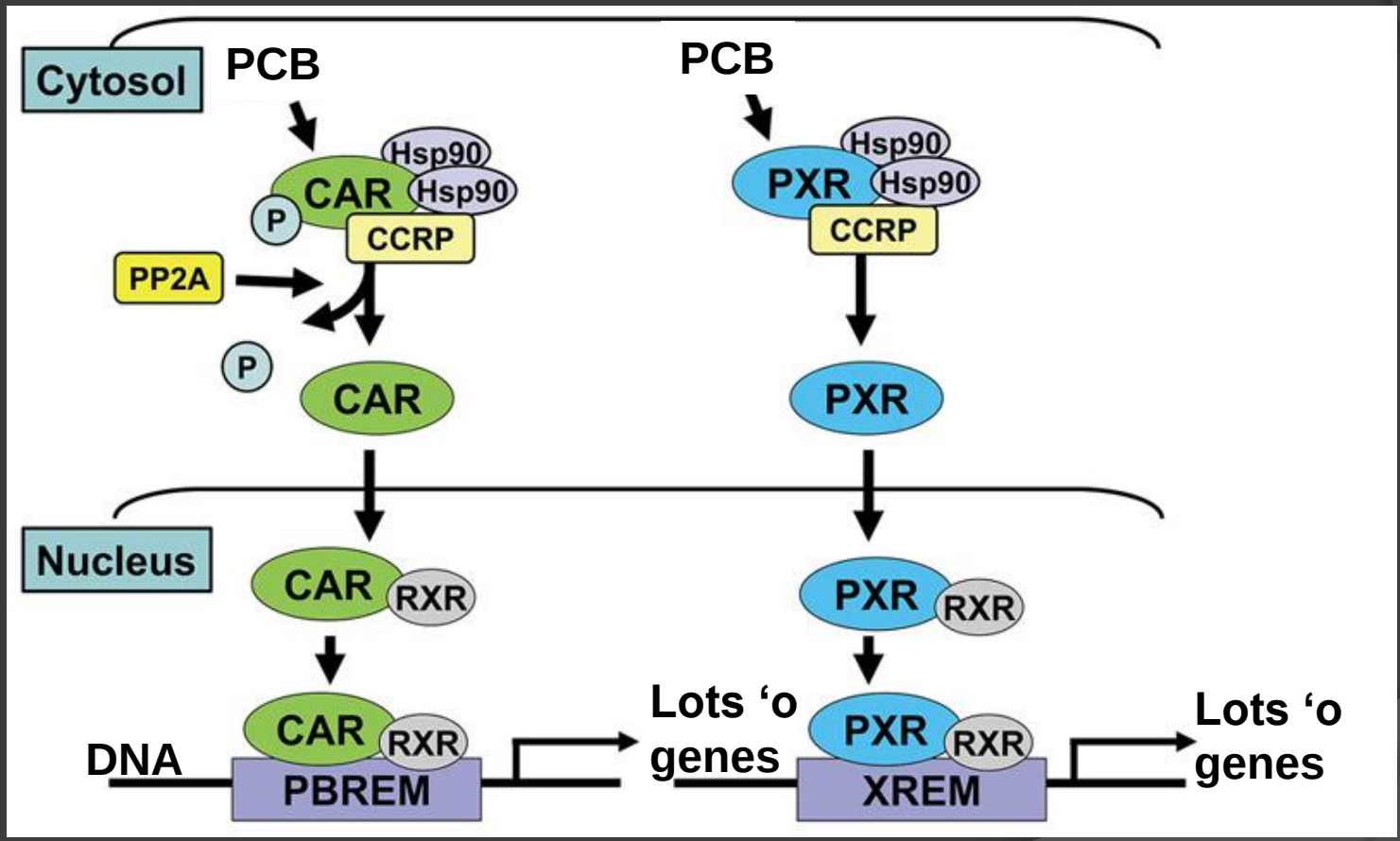
Non-Co-Planar PCBs Activate the Constitutive Adrostone Receptor (CAR) and the (PXR) and the Pregnane X Receptor



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PCBs and Endocrine and Reproductive Systems

- Altered thyroid gland structure (animals)
- Reduced thyroid hormone levels (animals and humans)(both co-planar and non-coplanar PCBs)
- Children born to mothers exposed to PCBs exhibit decreased gestational age and decreased birth weight.
- Reduced conception rates and live birth rates (non-human primates and other species)
- Reduced sperm counts (Rats)
- Reduced testosterone production in boys (which may result in delayed puberty)

PCBs and Neurotoxicity

- Hyperactivity (non-human primates and humans)
- Impaired learning ability (non-human primates and humans)
- Decreased visual acuity (humans)
- Decreased verbal and memory test scores at 4 years old (human)
- Lower cognitive and attention scores (humans)
- Psychomotor development at 6, 12, and 24 months of age (human)
- Possible increased risk of Parkinson's Disease

PCBs and Immunity

- Co-planar PCBs activate the AhR which is critical to development of the entire gut immune system and contributes significantly to inflammation and defense against cancerous cells.
- Decreased thymus size (infant monkeys). (The thymus generates T lymphocytes)
- Reduced ability of children to generate protective antibody responses following vaccination with standard childhood vaccine (i.e., tetanus and diphtheria toxoids)
- Decreased resistance to Epstein-Barr virus and other infections (rodents)

- Overall end result: Immunosuppression

PCBs and Cancer

- Co-planar PCBs activate the AhR which has been implicated in several cancers.
- Every commercial mixture of PCBs (Aroclors 1016, 1242, and 1254) causes cancer in the 2 year rat bioassay.
- Human epidemiological studies implicate PCBs in melanomas, liver cancer, gall bladder cancer, biliary tract cancer, gastrointestinal tract cancer, non-Hodgkin's lymphoma and brain cancer[5]
- PCBs that accumulate in sediment and bioaccumulate, for example, in fish are likely to be the most carcinogenic*

- Conclusion: Both co-planar and non-co-planar PCBs are human carcinogen[1, 2, 3,4]

[1]U.S. EPA
[2]International Agency for Research on Cancer (IARC)
[3] National Toxicology Program/NIEHS (NTP)
[4]National Institute of Occupational Health (NIOSH)
[5]American Toxic Substances Disease Registry (ATSDR)

Helpful Links

- EPA website on PCBs: http://www.epa.gov/epawaste/hazard/tsd/pcbs/
- IARC upgrades PCBs to “known carcinogens”: http://www.carexcanada.ca/en/announcements/PCBs_IARC_upgrade/
- PCBs and hypothyroidism: http://www.bio.umass.edu/biology/zoeller/pdf/chap33.pdf
- PCBs and decreased responses to childhood vaccines: http://www.nytimes.com/2006/09/05/science/05immu.html?_r=0
- PCBs and neurotoxicity: http://www.ncbi.nlm.nih.gov/pubmed/8725628

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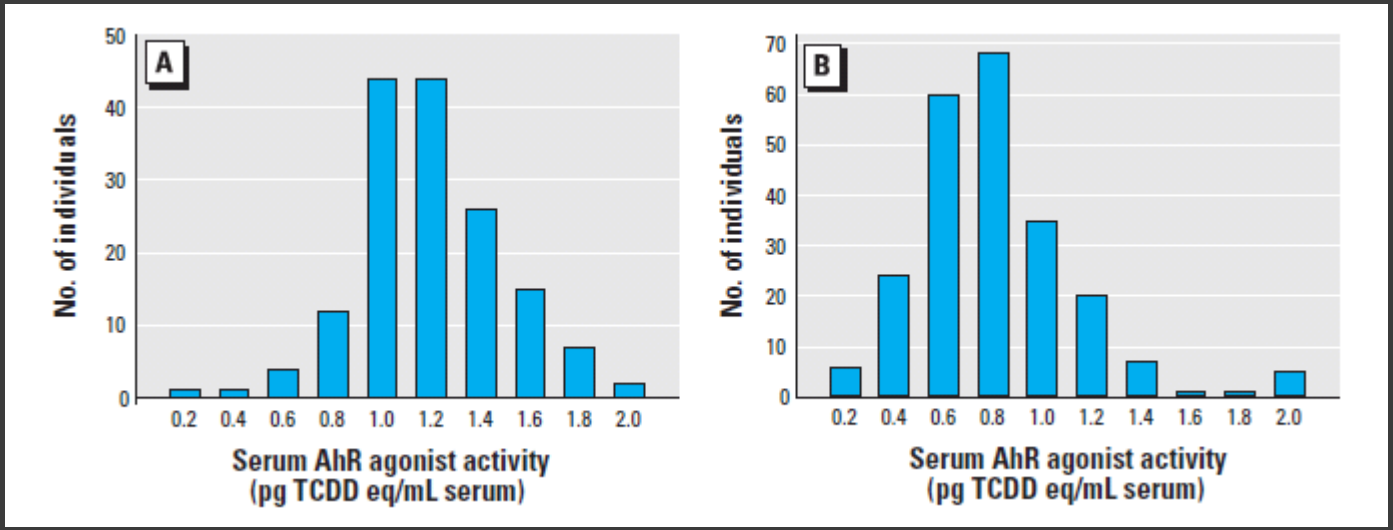

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